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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/572,796	03/21/2006	Christian Steinkuhler	ITR0060YP	5306

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MERCK AND CO., INC
P O BOX 2000
RAHWAY, NJ 07065-0907

EXAMINER	
CHOWDHURY, IQBAL HOSSAIN	

ART UNIT	PAPER NUMBER
1652	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/572,796	STEINKUHLER ET AL.	
	Examiner	Art Unit	
	Iqbal H. Chowdhury, Ph.D.	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 April 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4,5,7,9,11,13-18,20,22 and 24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-2, 4-5, 7, 9, 11, 13-18, 20, 22, 24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Application Status

Claims 1-2, 4-5, 7, 9, 11, 13-18, 20, 22 and 24 are pending.

In response to a previous Office action, a non-final requirement (mailed on 1/26/2007), Applicants filed a response and amendment received on 4/30/2007, amending claims 1, 4-5, 7, 9, 11, 15-18, 20, and 22, and canceling claims 8, 10, 12, and 19 is acknowledged. Claims 3, 6, 21, 23 and 25 remain cancelled.

Claims 1-2, 4-5, 7, 9, 11, 13-18, 20, 22 and 24 are under consideration and will be examined herein.

Applicants' arguments filed on April 30, 2007, have been fully considered but are not deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Maintained - Claim Rejections - 35 U.S.C. § 112

Previous rejection of Claims 1-2, 4-5, 7, 9, and 20 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is maintained. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection has been described at length in previous Office Actions. Applicant's amendments to claims 1, 4-5, 7, 9, 20 and 22, and arguments have been fully considered but are not deemed persuasive for the following reasons.

Claims 1, and 20 are directed to a synthetic nucleic acid molecule comprising a sequence of nucleotides that encodes a mammalian human heparanase protein, the sequence of nucleotides comprising two consensus cleavage sites recognized by an endoproteinase, as the cleavage sites are selected from the group consisting of: tobacco etch virus (TEV) protease cleavage sites, and wherein the cleavage sites are located between nucleotides encoding residues 100 and 168 of the heparanase protein, wherein the consensus cleavage sites are located before residues G 110 and K15 8 of the human heparanase protein and a method of expressing human heparanase in non-mammalian cells comprising transforming or transfecting non-mammalian cells with a vector comprising said nucleic acid sequence, culturing the host cell under conditions which allow expression of said human heparanase protein; disrupting the cells and at least partially purifying the human heparanase protein; and exposing the at least partially purified human heparanase protein to the endoproteinase, wherein the heparanase protein is cleaved at the consensus cleavage sites by the endoproteinase.

Applicants argue that Applicants note that the cited claims are amended herein to limit the claimed sequences to human heparanase sequences, which have been engineered in a specific manner to allow expression of biologically active human heparanase in non-mammalian cells and the nucleotide and amino acid sequences of wild-type human heparanase are known in the art, and the active form of heparanase was previously proposed to be a heterodimer between a 50 kDa C-terminal fragment and an 8 kDa N-terminal fragment, arising from the excision of an intervening 6 kDa peptide by unidentified proteolytic enzyme(s). Applicants also argue that the human heparanase sequence, as described in claim 1 and method claim 20, was modified by Applicants to contain consensus cleavage sites recognized by a specific known protease, which

allows the excision of a 6 kDa "intervening fragment" by the known protease, leading to biologically active heparanase and the human heparanase sequence, as described in claim 11 and method claim 22, was modified by Applicants to encode the 8 kDa N-terminal fragment and the C-terminal 50 kDa fragment, separated by a heterologous linker, wherein said nucleic acid molecule encodes a form of human heparanase that is constitutively active. Applicants further argue that the cited claims are limited to human heparanase sequences which contain specific modifications that allow expression of biologically active enzyme in heterologous expression systems and as such, Applicants submit that the rejection under § 112, first paragraph, as failing to comply with the written description requirement, is overcome.

Applicant's arguments and amendments to claims have been fully considered but are not deemed to be persuasive to overcome the rejection on Written description issues. Examiner acknowledges amendment to the claims, however the amendment does not give enough structural feature of any human heparanase encoded by the synthetic nucleic acid molecule or used in the claim method, which is required for fulfilling written description requirements. As discussed in the written description guidelines the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. A representative number of species means that the species,

which are adequately described are representative of the entire genus. **Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.** Satisfactory disclosure of a representative number depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of species disclosed. For inventions in an unpredictable art, adequate written description of a genus, which embraces widely variant species, cannot be achieved by disclosing only one species within the genus. The specification teaches a single representative species of SEQ ID NO: 19, which encodes a polypeptide of SEQ ID NO: 16 of said human heparanase protein. The genus of polypeptide of human heparanase encoded by synthetic nucleic acid molecule is structurally diverse as it broadly encompasses many mutants and variants having different structures. As such, the disclosure solely of functional features present in all members of the genus is insufficient to be representative of the attributes and features of the entire genus. Therefore, the rejection is maintained.

Maintained - Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Previous rejection of claims 1-2, 4-5, 7, and 20 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a synthetic nucleic acid molecule of SEQ ID NO: 19 comprising a sequence of nucleotides that encodes a human heparanase protein of SEQ

ID NO: 16, does not reasonably provide enablement for a synthetic nucleic acid molecule comprising a sequence of nucleotides that encodes any human heparanase protein is maintained. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. This rejection has been discussed at length in the previous office action. It is maintained for the reasons of record and discussed below.

Applicants argue that the Supreme Court has interpreted the enablement requirement as one of skill in the art is able to practice the claimed invention without undue or unreasonable experimentation and applicants submit that the full scope of the present claims is enabled by applicants specification because one of skill in the art would be able to practice the claimed invention without undue experimentation. Applicants also argue that the claims, as amended, are limited to human heparanase sequences with specific engineered modifications, and at the time of filing the present application, the wild-type nucleotide and amino acid sequences of human heparanase were known and available in the art. Applicants further argue that the specification provides ample guidance to one of skill in the art to modify these wild-type sequences and the determination of wild-type heparanase sequences allowed the recombinant expression of human heparanase; however, before the instant invention, it was not possible to express high levels of stable, correctly processed, recombinant human heparanase in non-mammalian cells. Furthermore, applicants argue that although it was postulated in the art that the active form of heparanase consists of a heterodimer between an N-terminal 8kDa fragment and a C-terminal 50 kDa fragment of heparanase, it was unknown what proteolytic enzyme was responsible for excising the 6 kDa intervening fragment and attempts to express recombinant human heparanase

in heterologous non-mammalian expression systems led to protein expression, but the resulting protein was not biologically active and if active heparanase could be obtained by purifying the processed protein from human cells, but yields of endogenous heparanase were very low, wherein applicants solved the problems of expressing high-levels of biologically active recombinant heparanase in heterologous non-mammalian expression systems. Applicants further argue that the specific guidance in that regard can be found, *inter alia,* on page 11, lines 4-21, and in Examples 2-7 and using the current specification as a guide, in conjunction with human heparanase sequences well known in the art, production of a synthetic nucleic acid molecule in accordance with the invention could be easily accomplished by one of skill in the art.

Applicant's arguments have been fully considered but are not deemed persuasive to overcome the rejection. The examiner acknowledges the amendment to the claims but disagrees with the applicant's contention that the claimed invention is adequately described. Claims 1 and 20 are still so broad as to encompass a synthetic nucleic acid molecule comprising a sequence of nucleotides that encodes any human heparanase protein. Claims still read on any human heparanase without any structural feature. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number genes encoding any human heparanase enzymes including many mutants and variants broadly encompassed by the claims. The specification discloses only a few human heparanase, which is insufficient to adequately describe the required genus of any human heparanase having heparan sulfate degrading activity.

Applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the

claims broadly including a synthetic nucleic acid molecule comprising a sequence of nucleotides that encodes any mammalian heparanase protein from any source. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of any heparanase enzyme having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). Therefore, the rejection is maintained.

Maintained-Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Previous rejection of Claims 1-2, 4-5, 7, 9, 11, 16-18, 20 and 22 under 35 U.S.C. 102(b) as being anticipated by Heinrikson et al. (US Patent 6,387,643 B1 published on 5/14/, 2002, claimed priority of US Provisional Application 60/075,706, filed on 2/24/1998) is maintained. Instant claims are drawn to a synthetic nucleic acid molecule comprising a sequence of nucleotides that encodes a mammalian heparanase protein comprising 8 kDa and 50 kDa protein fragment having two cleavage sites of endoproteinase located between amino acid residues 100 and 168 of the heparanase protein, a vector, host cell and a method of expressing mammalian

heparanase, purification and cleavage of the heparanase by endoproteinase.

Applicants argue that In order to anticipate a claim, prior art must contain all of the essential limitations of the claim and for prior art to anticipate under § 102 it has to meet every element of the claimed invention and applicants submit that the cited claims are not anticipated by Heinrikson et al. Applicants also argue that the cited claims require nucleic acid molecules encoding *specific, modified* forms of human heparanase and Heinrikson discloses the nucleotide sequence of unmodified, human heparanase, while the wild-type heparanase sequence disclosed in Heinrikson comprises consensus cleavage sites recognized by an endoproteinase, it is unknown which endoproteinase recognizes the cleavage sites of the wild-type protein. Applicants further argue that Heinrikson fails to teach a nucleic acid molecule comprising a sequence of nucleotides that encodes a human heparanase protein that is engineered to contain two consensus cleavage sites recognized by a specific, known protease, including thrombin protease cleavage sites, as required by claims 1 and 20 and Heinrikson also fails to teach nucleic acid molecules encoding the N-terminal 8kDa fragment of heparanase and the C-terminal 50 kDa fragment of heparanase, connected by a heterologous linker, as required by claims 11 and 22. Applicants argue that wild-type pro-heparanase nucleotide sequence that encodes the 8 and 50 kDa fragments of human heparanase joined by the natural 6kDa intervening fragment is not active until further processing occurs and state that neither disclosure teaches or suggests the cleaving of purified human heparanase by thrombin. And further state that in Heinrikson column 15, lines 1-6, where it is recite that human platelets were "stimulated with 1 U/ml thrombin for 5 min at 37° C." It is further recites that "[t]his concentration of thrombin has been reported to release 100% of the heparanase activity from platelets and this

disclosure of thrombin clearly describes the use of thrombin to release heparanase from platelets at the cell surface. Use of thrombin, in this instance, would not lead to processing of heparanase because thrombin cleavage sites are not present at the boundary of the 6 kDa "intervening fragment" in naturally occurring heparanase.

Applicant's arguments have been fully considered but are not deemed to be persuasive to overcome the rejection.

Heinrikson et al. indeed teach a modified human heparanase (p10, lines 35-50) and cleavage by thrombin. Although, thrombin was used in a crude platelets but whenever, heparanase comes in contact with thrombin, thrombin would cleaves the heparanase at all cleaving sites which is not restricted to only release from platelets but that released heparanase would be processed due to cleaving at the intervening sequence too having two cleavage sites, even though reference explicitly does not state that. Claim 11 and 22 recite a broad limitation "linker", which is reads on by leader sequence of Heinrickson et al., which is located between 8 and 50 kDa fragments. As discussed previously, Heinrikson et al. teach a fusion protein comprising human heparanase, which is 100% identical to SEQ ID NO: 15 and 99.9% identical to SEQ ID NO: 16, which encodes pro-heparanase protein having two cleavage sites for proteolytic cleaving propeptide to active processed heparanase protein, which is located at amino acid glu96-Ser97 and glu144-lys145 of human heparanase protein. Heinrickson et al. also teach a vector comprising said gene encoding human heparanase protein with leader sequence, host cell including yeast cell such as Pichia and S. cerevisiae as well as insect cell, mammalian cell, and method of producing human heparanase protein, and purification. Heinrikson et al. further teach endoproteinase such as thrombin and cleaving human heparanase by thrombin. Heinrickson et al.

Because the synthetic human heparanase of the instant application and that of the reference is one and the same, Examiner takes the position that the leader sequence which linked the 8 kDa and 50 kDa fragments disclosed in the reference inherently is the same linker sequence as claimed in claim 11, and 22. Since the Office does not have the facilities for examining and comparing applicants' synthetic protein having a specific linker sequence with the fusion protein produced by the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product (i.e. with linker sequence) and the product of the prior art (i.e., with leader sequence). See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald* et al., 205 USPQ 594. Therefore, Heinrikson et al. anticipate claims 1-2, 4-5, 7, 9, 11, 16-18, 20 and 22 of the instant application. Therefore, the rejection is maintained.

Withdrawn-Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Previous rejection of Claims 1-2, 4-5, 7-18, 20, 22 and 24 under 35 U.S.C. 102(b) as being anticipated by Levy-Adam et al. (Heterodimer formation is essential for heparanase enzymatic activity, Biochem Biophys Res Commun. 2003 Sep 5; 308(4): 885-91, see IDS) is withdrawn in view of applicants amendment of claims i.e. adding limitation of SEQ ID NO: 15 and 16, which is required for claims 11 and 22, and persuasive arguments i.e. Levy et al. do not teach explicitly that thrombin is used to cleave said pro-heparanase protein, which is required for

claims 1 and 20.

New-Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 15 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Heinrikson et al. (US Patent 6,387,643 B1 published on 5/14/, 2002, claimed priority of US Provisional Application 60/075,706, filed on 2/24/1998) as applied to claims 1-2, 4-5, 7, 9, 11, 16-18, 20 and 22 above, and further in view Washida et al. (Appl Microbiol Biotechnol, 2001). Instant claims are drawn to a synthetic nucleic acid molecule comprising a sequence of nucleotides that encodes a mammalian heparanase protein comprising 8 kDa and 50 kDa protein fragment linked by a linker of (Gly-Ser)3 having two cleavage sites of endoproteinase located between amino acid residues 100 and 168 of the heparanase protein.

Heinrikson et al. teach a fusion protein comprising human heparanase, which is 100% identical to SEQ ID NO: 15 and 99.9% identical to SEQ ID NO: 16, which encodes pro-heparanase protein having two cleavage sites for proteolytic cleaving propeptide to active processed heparanase protein, which is located at amino acid glu96-Ser97 and glu144-lys145 of human heparanase protein. Heinrickson et al. also teach a vector comprising said gene encoding human heparanase protein with leader sequence, host cell including yeast cell such as Pichia and S. cerevisiae as well as insect cell, mammalian cell, and method of producing human heparanase protein, and purification. Heinrikson et al. further teach endoproteinase such as thrombin and cleaving human heparanase by thrombin. Heinrickson et al. furthermore, teach fragments of human heparanase including 8 kDa and 50 kDa fragments and leader sequence which link 8 kda and 50 kDa protein fragment. Heinrickson et al. do not teach using (Gly-Ser) repeat as linker.

Washida et al. teach a spacer-mediated display of active lipase on the yeast cell surface by cell surface engineering, wherein the linker peptides (spacers) consisting of the Gly/Ser repeat sequence, including (Gly-ser)1, (Gly-Ser)2 and (Gly-ser)3, which is inserted at the C-terminal portion of lipase to enhance lipase activity by preserving the conformation of the active site near the C-terminal portion.

By combining the teachings of Heinrickson et al. and Washida et al., it would have been obvious to one to ordinary skill in the art at the time of the invention was made to replace leader sequence of Heinrickson et al. with (Gly-Ser) repeat linker/spacer of Washida et al. to produce a recombinant highly active heparanase protein after cleaving with endoproteinase such as thrombin.

One of ordinary skill in the art would have been motivated to use (Gly-Ser) repeat as linker/spacer because said linker enhances said enzyme activity by preventing the conformation active site near the C-terminal portion of said enzyme.

One of ordinary skill in the art would have a reasonable expectation of success because Washida et al. could successfully convert use (Gly-Ser) repeat linker ketoisophorone to levodione, an intermediate to actinol production.

Therefore, claims 15 and 24 would have been prima *facie* obvious to use of ordinary skill in the art.

Conclusion

Claims 1-2, 4-5, 7, 9, 11, 13-18, 20, 22 and 24 are pending.

Claims 1-2, 4-5, 7, 9, 11, 13-18, 20, 22 and 24 are rejected.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R. 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Iqbal Chowdhury, Ph.D. whose telephone number is 571-272-8137. The examiner can normally be reached on 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 703-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Iqbal Chowdhury, PhD Patent Examiner
Art Unit 1652 (Recombinant Enzymes)
US Patent and Trademark Office
Remsen Bldg., Rm. 2B69, Mail Box. 2C70
Ph. (571)-272-8137, Fax. (571)-273-8137

IC

PONNATHAPU ACHUTAMURTHY
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600